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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/938,754	08/24/2001	Samuel J. Danishefsky	2003080-0083 (SK-943-US)	4106
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24280 7590 09/10/2003

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Exchange Place
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Boston, MA 02109

EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/938,754

Applicant(s)

DANISHEFSKY ET AL.

Examiner

Brenda L. Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-56 is/are pending in the application.
- 4a) Of the above claim(s) 5,6,23,29,31,32,36,37 and 39-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,7-22,24-26,30,33-35 and 38 is/are rejected.
- 7) ☒ Claim(s) 27 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-56 are pending in the application.

Election/Restrictions

1. Applicant's election of Group I in Paper No. 17 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 5, 6, 23, 29, 31, 32, 36, 37 and 39-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 17.
3. Claims 1-3, 7-21, 24, 30, 33-35 and 38 are rejected as being drawn to an improper Markush group. The recited compounds, while possessing a common utility, differ widely in structure and are not art-recognized equivalents and are thus, independently distinct for the reasons set forth in the restriction. The Markush group represented by the variable X has variably different definitions, rendering the claims clearly improper.

Specification

4. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The

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amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 30, 33-35 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims are not adequately enabled solely based on its inhibitory effect on the Hsp90 molecular chaperone provided in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, which call for the treatment of cancer. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to treat cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our

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present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See *In re Ruskin*, 148 USPQ 221; *Ex parte Jovanovics*, 211 USPQ 907; MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1-4, 7-22, 24-28, 30, 33-35 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

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claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1-4, 7-21, 30, 33-35 and 38 are vague and indefinite in that it is not known what is meant by the moiety "a protecting group" in a compound claim.

Protecting groups in a process claim may be necessary to protect a functional site from the reaction and are then removed. The compound in a compound claim must be described in its entirety, protecting group does not set forth the metes and bounds of the variables R_A , R_B , R_C , R_D , R_E , R_F , R_J , R_7 , R_K and R_L .

b) Claims 1-4, 7-21, 30, 33-35 and 38 are vague and indefinite in that it is not known what is meant by the moiety $-C(O)NR_K$ in the definition of R_7 , which is not valence satisfied.

c) Claims 1-4, 7-21, 30, 33-35 and 38 are vague and indefinite in that it is not known what is meant by analogues of radicicol and monocillin or analogues of geldanamycin. Analogues implies more than what is positively recited. See line 6 on page 89 **and** lines 5-6 on page 90 within the proviso.

d) Claims 1-4, 7-21, 30, 33-35 and 38 are vague and indefinite in that it is not known what is meant by the moieties alkylene and carbonyl in the definition of R_L within the proviso at the end of the claim. Alkylene and carbonyl are divalent moieties and R_L is a monovalent substituent.

e) Claims 1, 22 and 24-26 do not end with a period.

608.01(m) Form of Claims [R - 3]

The claim or claims must commence on a separate sheet and should appear after the detailed description of the invention. < While there is no set

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statutory form for claims, the present Office practice is to insist that each claim must be the object of a sentence starting with "I (or we) claim", "The invention claimed is" (or the equivalent). If, at the time of allowance, the quoted terminology is not present, it is inserted by the clerk. **Each claim** begins with a capital letter and **ends with a period**. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, >36 USPQ2d 1211< (D.D.C. 1995). ** >Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation, 37 CFR 1.75(i).

- f) Claim 19 recites the limitation "-OSO₂R_j" in the definition of R₅ and R₆.

There is insufficient antecedent basis for this limitation in the claim.

- g) Claim 24 is vague and indefinite in that it is not known what is meant by the double bond in the structure near the chlorine atom.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4, 7, 13, 18 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Mirrington et al., Tetrahedron Letters. Mirrington teaches the compounds of the instant invention where Z is O; X is O; A and B together are oxireno; R₅ and R₆ are H; D and E together are –CH₂–CH₂–; G and J together are –CH₂–CH₂–; K and L together are C=O; R₁ is Cl; R₂ is OH or OMe; R₃ is H; and R₄ is OH or OMe. See formula II where R is H or Me.

8. Claims 1, 4, 13, 18, 21, 30, 33-35 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugimura et al., U.S. Patent 5,650,430 and 5,597,846. Sugimura teaches the compounds, compositions and method of use of the compounds of the instant invention where Z is O; X is O; A and B together are oxireno; R₅ and R₆ are H; D and E together are -CH=CH-; G and J together are -CH=CH-; K and L together are C=O; R₁ is Cl; R₂ is OR_B or O(C=O)R_B; R₃ is H; and R₄ is OR_D or O(C=O)R_D where R_B and R_D are arylalkyl, heteroaryl, etc.

9. Claims 1, 4, 7, 13, 18, 21 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Lampilas et al., Tetrahedron Letters. Lampilas teaches the compounds and compositions of the instant invention where Z is O; X is O; A and B together are oxireno; R₅ and R₆ are H; D and E together are -CH=CH-; G and J together are -CH=CH-; K and L together are C=O; R₁ is H or Cl; R₂ is OH or tert-butyldimethylsilyl; R₃ is H; and R₄ is tert-butyldimethylsilyl. See examples 12, 16, etc.

Claim Objections

10. Claims 27 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 703-305-1880. The examiner can normally be reached on 8:30-5:00 Monday - Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A handwritten signature in black ink that reads "Brenda Coleman". The signature is fluid and cursive, with a long horizontal stroke at the end.

Brenda Coleman
Primary Examiner Art Unit 1624
September 8, 2003